

REMARKS

I. Status of Claims.

Claims 1-13 are pending.

Claims 1, 2, 3, 5, 9 and 13 are amended in a manner that is believed to overcome rejections contained in the pending Office Action. The amendments to the claims have been made solely for reasons of clarity and not for reasons of prior art. Claim 8 has been cancelled without prejudice as being directed to duplicitous subject matter of amended claim 9. Claims 14 and 15 have been added to further emphasize Applicants' invention. Support for these amendments and added claims can be found throughout the drawings, specification and claims as originally filed. No new matter or issues are believed to be introduced by these amendments.

II. Rejection of claims 1, 3-6, 9 and 11-12 under 35 USC 112, first paragraph.

In the Office Action dated December 23 , 2004, the Examiner rejected claims 1, 3-6, 9 and 11-12 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner stated that the rejected claims are drawn to a method for modulating behavioral and neurological adaptive responsiveness to stress by applying to the central nervous system a therapeutically effective amount of an inhibitor of the DP VI enzyme. The Examiner further stated that the "instant specification fails to provide a clear definition of "psychophysiological effects of stress including anxiety." The Examiner stated that the instant specification, as filed, fails to provide any guidance on how to practice the claimed method or how to extrapolate the information within limited working examples to all recited pathological conditions or treatment of effects of stress in general, thus requiring undue experimentation. Applicants respectfully traverse this rejection.

Applicants have amended claims 1 and 2 to further define and clarify its invention. Applicants have provided multiple examples that contain specific criteria of behavioral and neurological adaptive responsiveness to dosing within various animals studies the results of which can be extrapolated for use in humans by those skilled in the art without undue experimentation. Applicants would again respectfully direct Examiner's attention to the

extensive specific criteria within Examples 1-4 that more than fully comply with the requirements of 35 USC 112, first paragraph. The criteria measured for dose response are also the criteria to be modulated. Applicants specifically direct Examiner's attention to the standard methodology used within Examples 1-4 to assess stress induced treatment response. With reference to the Examples it is noted that there are presented three standardized tests known in the art that measure behavioral and neurological adaptive responsiveness to stress which one might wish to modulate including a social interaction test, a stress induced body weight loss test and an anxiety in the social interaction test.

The use of a chemical compound for a particular disease state is routinely confirmed by establishing that it possesses properties of therapeutic value through the aforementioned tests conducted on standard experimental animals. Applicants have disclosed numerous examples and data on standardized laboratory animals, which can clearly be used by one skilled in the art to understand therapeutic utility. No undue experimentation is required to confirm the possession of such therapeutic effectiveness. As the Federal Circuit found In re Brana, 51 F.3d 1560, 1566, 34 U.S.P.Q. 2d 1436, 1441 (Fed. Cir. 1995), it is unnecessary for a patent applicant to even mention a specific disease as an alleged utility when a specification discloses purely in vitro and animal model test showing the efficacy of pharmaceutical compounds in the alleviation of tumors. In the instant case Applicants have more than provided ample evidence via animal models of the use of DPIV inhibitor applied to the central nervous system.

Applicants would also like to point out that the Patent and Trademark Office has the burden of showing that the disclosure entails undue experimentation. In Re Angstadt (CCPA 1976) 537 F.2d 498, 190 USPQ 214., It is respectfully submitted that the Patent Office has not carried this burden or provided the required reasonable basis for contending that one skilled in the art would not be able to practice the invention as claimed. Gould v. Mossinghoff 229 U.S.P.Q. 1, 13 (D.C. D.C. 1985). Accordingly, Applicants respectfully submit that any experimentation which might be required would not rise to the level of undue experimentation if the specification is interpreted by one skilled in the art.

As to Claim 1, there is no basis for the Examiner's opinion of lack of enablement, as is required to maintain such a rejection. Gould v. Mossinghoff, 229 U.S.P.Q. 1, 13-14 (D.D.C. 1985) aff'd in part, vacate in part, and remanded sub nom, Gould v. Quigg, 3 U.S.P.Q. 2d 1302

(Fed. Cir. 1987)("In examining a patent application, the P.T.O. is required to assume that the specification complies with the enablement provision of section 112 unless it has 'acceptable evidence or reasoning' to suggest otherwise"; the burden of persuasion is on the P.T.O.); In re Armbruster, 185 U.S.P.O. 152 (C.C.P.A. 1975).

The Examiner references neither the level of knowledge of "one of ordinary skill in the art," nor the nature of the impediments to enablement one might encounter. Applicants again respectfully call upon the Examiner to provide an affidavit under §104(d)(2) as to the reasoning under which enablement is questioned.

In the alternative, Applicants respectfully request that this rejection be withdrawn.

III. Rejection of Claims 1-13 under 35 USC 112, second paragraph.

The Examiner rejected claims 1-13 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of Applicants' invention.

A. DPIV-Like Enzyme: Claims 1 and 2 and their dependant claims were rejected under 35 USC 112, second paragraph for the term "DP IV –like" enzyme. The Examiner stated that it was not obvious, which enzymes are to be included or excluded by the limitation "like." Applicants respectfully disagree with the Examiner's rejection, however, in order to move the instant application to allowance Applicants have amended claims 1 and 2 as noted above and respectfully request that this rejection be withdrawn.

B. Other Substrate Sharing Properties: Further rejection was made to claim 2 for the recitation of "other substrates sharing similar properties." The Examiner stated that it was not clear what "other substrates" were intended by the claim. Applicants have amended claim 2 to more clearly define their invention. Applicants respectfully submit that this rejection has now been overcome.

C. Indefinite Claims: The Examiner rejected claims 3-5, 7-13 as being indefinite for being dependent from indefinite claims. Applicants have amended claims 1 and 2 as noted above and therefore respectfully submit that these rejections have been overcome as well.

IV. Rejection of claims 2, 7-8, 10 and 13 under 35 USC 102(b).

The Examiner rejected claims 2, 7-8, 10 and 13 under 35 USC 102(b) as being anticipated by Powers et al. (WO 95/2961, 1995, Document BL, IDS of Paper No. 2) (“Powers”). Applicants respectfully traverse this rejection.

A. Examiner’s Rejection: The Examiner’s rejection stated that Powers discloses administration of inhibitors of dipeptidyl peptidase IV and such administration leads to the decrease of enzymatic activity of DPIV and consequently to reduction of degradation of its natural endogenous substrate.

B. Applicants’ Claimed Invention: Applicants’ claimed invention as described in amended claim 2, from which all subsequent claims depend, is directed to the “treatment of anxiety” as a central nervous system disorders. Applicants claimed method of treating central nervous system disorders such as anxiety is by the administration of DP-IV inhibitors to the central nervous system.

C. Disclosure of Powers: Power discloses the use of peptidyl derivative of diesters of α -aminoalkylphosphonic acids, particularly those with proline or related structures, their use in inhibiting serine proteases with chymotrypsin-like, elastase-like, and dipeptidyl peptidase IV specificity. The disclosure of Powers is directed to the use of DPIV inhibitors as anti-inflammatory agents, anticoagulants, anti-tumor agents, and anti-AIDS agents. Powers does not disclose applying DPIV inhibitors to the “central nervous system” for the treatment of anxiety.

D. Deficiencies of Powers: Claim 2 as amended, from which all rejected claims depend, is directed to the “treatment of anxiety” as a central nervous system disorders. Unlike Applicants’ claimed invention, Powers is completely devoid of any disclosure of the use of DP-IV inhibitors for the treatment of central nervous system disorders and specifically any teaching of “applying to the central nervous system” a therapeutically amount of DP-IV inhibitors, as Applicants have disclosed and claimed. Powers does not disclose the use of DPIV inhibitors within the central nervous system. Given Applicants’ method of applying DPIV inhibitors to the central nervous system and the absence of an anticipatory teaching in Powers, Applicants respectfully request that this rejection be withdrawn.

VII Rejection of claims 1, 3-6, 9 and 11-12 under 35 USC 102(b).

The Examiner rejected claims 1-13 under 35 USC 102(b) as being anticipated by Powers et al. (WO 95/2961, 1995, Document BL, IDS of Paper No. 2) (Power).

A. Examiner's Rejection: The Examiner's rejection stated that Powers discloses inhibitors of dipeptidyl peptidase IV and their use of administration as anti-inflammatory agents, anticoagulants, anti-tumor agents and anti-AIDS agents. Administration of a therapeutic amount of inhibitors of Powers leads to the decrease of enzymatic activity of DPIV and consequently to the reduction of degradation of its natural endogenous substrate. As such, the Examiner reasoned, the administration of DPIV inhibitors as disclosed by Powers leads to reduction in stress responsiveness and anxiety.

B. Applicants' Claimed Invention: Applicants' claimed invention as set forth in amended claim 1 from which the other rejected claims depend, is directed to the "treatment of psychophysiological effects of stress" resulting from central nervous system disorders such as anxiety. Applicants' claimed invention is directed to the beneficial neurological and psychophysiological effects that result from the inhibition of DPIV within the central nervous system by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" (emphasis added). Furthermore, as shown in examples 3 and 4, Applicants' invention is directed to the beneficial neurological effects that result from the inhibition of DP IV within the central nervous system by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" alone or in combination with NPY (claim 5). The outstanding beneficial effect of this combination is shown in particular in examples 3 and 4.

C. Disclosure of Powers: Power discloses the use of peptidyl derivative of diesters of α -aminoalkylphosphonic acids, particularly those with proline or related structures, their use in inhibiting serine proteases with chymotrypsin-like, elastase-like, and dipeptidyl peptidase IV specificity and their roles as anti-inflammatory agents, anticoagulants, anti-tumor agents, and anti-AIDS agents. Powers does not disclose, however, applying DP-IV inhibitors to the "central nervous system." The use of DP-IV inhibitors through the blood brain barrier is not disclosed in Powers.

D. Deficiencies of Cited References: Unlike Applicants' claimed invention, Powers does not disclose the "treatment of anxiety" resulting from central nervous system disorders using an inhibitor of DP IV. Powers also does not disclose the treatment of anxiety by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" alone or in combination with NPY. It is made clear throughout the description of the present invention that the therapeutic targets of the present invention are the receptors of neuropeptides. The main target is the neuropeptide Y receptor Y1. These receptors are localized in the central nervous system (brain) of mammals. As it is known in the art, the central nervous system is a separate compartment of the body/organism of mammals, which is strongly demarcated from the rest of the body by the so called "blood-brain-barrier." Accordingly, the claims of the present invention specify inhibition of dipeptidyl peptidase IV (DP IV) activity by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" in order to reach the desired pharmaceutical target. Powers does not disclose "applying to the central nervous system a therapeutically effective amount of a competitive inhibitor of the dipeptidyl peptidase (DP IV) as Applicants have disclosed and claimed. The inhibition of DPIV within the teachings of Powers does not occur within the central nervous system.

As has been clearly enunciated by the Federal Circuit: Anticipation requires the presence in a single prior art reference the disclosure of each and every element of the claimed invention, arranged as in the claim. Lindermann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 221 USPQ 481, 485 (Fed Cir. 1984) (emphasis added). Here the requirement of showing each and every element of Applicant's claimed invention in a single prior art reference has not been met since Powers fails to disclose Applicants' claimed invention of applying to the central nervous system DPIV inhibitors as detailed above. In light of the above, it is respectfully submitted that the 35 U.S.C. §102(b) is improper, may be properly withdrawn, and Applicants so request.

VII. Rejection of claims 1-13 under 35 USC 102(e).

The Examiner rejected claims 1-13 under 35 USC 102(e) as being anticipated by Demuth et al., U.S. Patent No. 6,319,893 (Demuth '893). Applicants respectfully traverse this rejection.

A. Examiner's Rejection: The Examiner stated that Demuth '893 describes the administration to a mammal of therapeutically effective amounts of an inhibitor of DPIV. The Examiner further stated that Demuth '893 also discloses methods of administration (parenterally, orally), pure forms of inhibitors, and formulations with physiologically acceptable adjuvants.

B. Applicants' Claimed Invention: Applicants' claimed invention as set forth in the claims is directed to the "treatment of anxiety" resulting from central nervous system disorders. The instant claims are directed to methods of treating these central nervous system disorders such as anxiety through the administration of DP-IV inhibitors by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" alone or in combination with NPY.

C. Disclosure of Demuth '893: Demuth '893 discloses a method of raising the blood sugar level in a mammal having hypoglycemia. The method disclosed in Demuth '893 reduces degradation of glucagons by administering to the mammal a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV and physiologically acceptable adjuvants and/or excipients. Demuth '893 does not disclose applying DPIV inhibitors to the central nervous system as Applicants have disclosed and claimed.

D. Deficiencies of Demuth '893: Demuth '893 is completely devoid of any disclosure related to DP-IV inhibitors for the treatment of central nervous system disorders through the use of DP IV inhibitors by "applying to the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" alone or in combination with NPY. The inhibition of DPIV within the teachings of Demuth '893 does not occur within the central nervous system. Applicants respectfully request that this rejection be withdrawn.

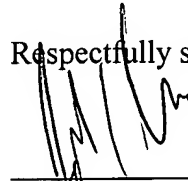
VIII. Rejection of claims 1-13 under Obviousness-type Double Patenting.

A rejection was made to claims 1-13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,319,893 (Demuth '893). Applicants respectfully but vigorously suggest that the claimed subject matter of the rejected claims differ from that of the claims of Demuth '893, as discussed immediately above. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

The claims remaining within the application are believed to patentably distinguish over the prior art and to be in condition for allowance. Early and favorable consideration of this application is respectfully requested.

Respectfully submitted,



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Dated: March 23, 2005